AWARD NUMBER: W81XWH-12-2-0015

TITLE: NRC/AMRMC Resident Research Associateship Program

PRINCIPAL INVESTIGATOR: Dr. Michael Dubick

CONTRACTING ORGANIZATION: National Academy of Sciences Washington, DC 20001

REPORT DATE: March 2015

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

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6. AUTHOR(S) Dr. Michael Dubi	ck			5d.	PROJECT NUMBER
email: michael.a.d	dubick.civ@mail.mil			5e.	TASK NUMBER
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of 5 applications we A total of 6 Associa	ere received during th	te period and of these, e during the reporting	5 were reviewed by	NRC panels. 4 av	through a broad outreach plan. A total ward offers were made and 4 accepted. reports. The productivity of these
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REPORT DOCUMENTATION PAGE

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National Research Council RESEARCH ASSOCIATESHIP PROGRAM with U.S. Army Medical Research & Materiel Command

Annual Contract Technical Report

Contract No. W81XWH-12-2-0010 Contract Period: 02/06/2012-02/05/2017

Contract No. W81XWH-12-2-0015 Contract Period: 03/01/2012-02/28/2017

Contract No. W81XWH-12-2-0018 Contract Period: 03/15/2012-03/14/2017

Contract No. W81XWH-12-2-0030 Contract Period: 03/15/2012-03/14/2017

Contract No. W81XWH-12-2-0033 Contract Period: 05/01/2012-04/30/2017

Report Period: 05/01/2014-04/30/2015

During the reporting period, the NRC conducted the following activities in support of the subject contract:

Outreach and Promotion

The promotional schedule to advertise the National Research Council (NRC) Research Associateship Programs included the following: 1) attendance at meetings of major scientific and engineering professional societies; 2) advertising in programs and career centers for these and other professional society meetings; 3) direct mailing and emailing of announcements and program materials to presidents, graduate deans, and heads of appropriate science and engineering departments and minority-affairs offices of all academic degree-granting institutions in the United States; 4) posting announcements on internet job sites, electronic newsletters and professional society websites; 5) print advertising in high profile publications (e.g., Science magazine, the Chronicle of Higher Education); and, 6) maintaining a presence on social media sites such as Facebook.

The NRC attended a number of minority focused events in which we maintained exhibit booths, participated in workshops and advertised in meeting literature, newsletters and websites or submitted materials for distribution. In addition, ads were placed in a variety of minority publications (e.g., Affirmative Action, Black Collegian).

In advertising the Research Opportunities available to prospective applicants, the NRC maintained an up-to-date listing of all active Research Advisers, current Adviser contact information and details of each Research Opportunity.

Processing and Review of Applications

Applications to the Research Associateship Program were submitted via a web-based application system. Each of the four application cycles opened two months prior to the application deadline. NRC staff provided support to prospective applicants including providing application instructions, technical support and additional information as requested.

A summary of applications for the reporting period is shown in Table 1.

For each applicant, the NRC received and processed an application form, a research proposal, transcripts, a statement of previous and current research, and confidential reference reports. An application file check was made prior to the review and each applicant was notified if required documents were missing.

The NRC convened panels in five broad discipline areas for the competitive review of applications in the Research Associateship Programs. Results of the review were made available to Laboratory Program Representatives immediately following the conclusion of the each review.

A summary of the outcome of the review of applications for the reporting period is shown in Table 1.

Administration of Awards

The NRC made awards to applicants based on sponsor authorization. A summary of awards authorized and the acceptance or declination by the applicant during the current reporting period is shown in Table 1.

For Associates beginning or continuing tenure, the NRC provided the administrative functions described in the contract Statement of Work. These functions included stipend payments, management of a major medical benefits insurance program, and reimbursement for relocation and travel to professional meetings.

A summary of NRC Research Associates on tenure during the reporting period is shown in Table 2.

Outcomes Reporting

All NRC Associates who completed tenure were required to submit a final report that described the outcome of their Associateship award. Final reports received by the NRC during the current reporting period are attached to this technical report.

The activities of Associates submitting final reports during this reporting period, including publications, presentations and patents, as well as an assessment of their experience in the program, are summarized in Table 3. Specific research accomplishments of Associates completing tenure during the reporting period are summarized in Table 4.

Table 1. Applications and Awards

Table 2. Associates on Tenure

Table 3. Associates Activity

Table 4. Summary of Associate Research

Attachments: Associate Final Reports

	May 2014	Aug 2014	Nov 2014	Feb 2015	Total
TOTAL APPLICATIONS	5	9	5	7	26
Applications not reviewed	1	3	1	0	5
Applications reviewed	4	6	4	7	21
Not recommended	0	1	0	0	1
Recommended	4	5	4	7	20
Withdrawn	0	0	0	0	0
Lab decision pending	0	1	0	3	4
Awards offered	2	3	3	3	11
Applicant decision pending	0	0	0	0	0
Awards accepted	2	3	2	3	10
Awards declined	0	0	1	0	1
Not funded	2	1	1	1	5

Table 2: Associates on Tenure

Associate	Adviser	Tenure Dates	Final Report
U.S. Army Institute of Surgical Research	h		
Benov, Avi	Darlington, Daniel Norman	8/1/2014-7/31/2015	
Cheppudira, Bopaiah Pooviah	Clifford, John L	9/4/2012-9/3/2015	
Choi, Jae hyek	Wang, Heuy-Ching H.	11/15/2011-11/14/2015	
Greene, Whitney Ann	Wang, Heuy-Ching H.	4/25/2012-7/24/2015	
Hurtgen, Brady Joe	Wenke, Joseph C	12/3/2012-9/18/2014	Received
Kaini, Ramesh Raj	Wang, Heuy-Ching H.	1/3/2013-1/2/2016	
Karna, Sai Lakshmi Rajasekhar	Leung, Kai P	4/1/2013-4/13/2016	
Kreyer, Stefan Franz Xaver	Batchinsky, Andriy I	12/7/2012-5/31/2014	Received
Miller, Christine Lindsay	Leung, Kai P	2/4/2013-2/3/2016	
Nyland, Jennifer Elaine	Clifford, John L	2/1/2013-12/31/2014	Received
Olekson, Melissa Ann	Leung, Kai P	9/2/2014-9/1/2015	
Parida, Bijaya Kumar	Dubick, Michael A.	3/19/2012-3/18/2016	
Penn, Alexander Hayes	Torres, Ivo P	1/14/2015-1/13/2016	
Pilia, Marcello	Rathbone, Christopher R	9/4/2012-2/6/2015	Received
Rose, Lloyd Frederick	Leung, Kai P	11/1/2012-10/31/2015	
Salas, Margaux Marie	Clifford, John L	10/10/2012-10/9/2015	
Sanchez, Carlos Jose	Wenke, Joseph C	9/7/2011-9/6/2014	Received
Sosanya, Natasha	Gibbons, Robert V	4/20/2015-4/19/2016	11000.100
Van Laar, Tricia Annette	Leung, Kai P	4/9/2012-10/8/2015	
Ward, Catherine Lindsey	Wenke, Joseph C	8/22/2011-9/4/2014	Received
U.S. Army Medical Research Institute of		0/22/2011-9/4/2014	Received
Hubbard, Kyle	McNutt, Patrick Michael	6/1/2012-5/31/2015	
U.S. Army Medical Research Institute of		0/1/2012 0/01/2010	l l
Bernhards, Robert Cory	Welkos, Susan Lee	7/11/2013-7/10/2015	
Cohen, Courtney Alicia	Glass, Pamela J	7/28/2014-7/27/2015	
DeWald, Lisa Marie	Glass, Pamela J	5/7/2012-5/6/2015	
Duy, Janice	Minogue, Timothy Devins	8/1/2013-7/31/2015	
Friedrich, Brian Michael	Hensley, Lisa E.	8/1/2011-6/18/2014	Not Recv'd
Haddow, Andrew Douglas	Turell, Michael J	4/15/2014-11/30/2014	Received
Harrell, William Ayers	Smith, Leonard Alan	3/29/2011-3/28/2015	Not Recy'd
Huse, Valerie	Minogue, Timothy Devins	9/29/2014-9/28/2015	1401110011
Maes, Piet	Hooper, Jay W.	12/3/2012-6/2/2014	Received
O'Hearn, Aileen E	Schoepp, Randal J.	4/1/2013-3/31/2016	Received
·		3/1/2011-10/5/2014	Received
Rahman, Md. Mizanur Smith, Jessica L	Ahmed, Syed Ashraf		Received
	Ulrich, Robert Glenn	6/24/2013-6/23/2015 1/2/2014-1/1/2016	
Stefan, Christopher Patrick	Minogue, Timothy Devins		
Stojadinovic, Marija	Panchal, Rekha G.	12/1/2014-11/30/2015	Received
Stonier, Spencer William	Dye, John Michael	8/1/2011-6/30/2014	Received
Tursiella, Melissa Lynne	Schmaljohn, Connie	4/1/2014-3/31/2016	
Walter Reed Army Institute of Research		2/44/2044 2/40/2046	
Anderson, Margery Diane	Yourick, Debra Lynn	3/11/2014-3/10/2016	Received
Caudle, Krista Layne	Tortella, Frank Casper	1/28/2013-7/13/2014	Received
Kobylinski, Kevin Conrad	Szumlas, Daniel Edward	10/17/2011-10/16/2015	
Linton, Yvonne-Marie	Clark, Jeffrey William	10/3/2011-10/2/2015	
McCracken, Michael Kevin	Jarman, Richard George	3/9/2015-3/8/2016	
Pichard, Luis Eduardo	Balkin, Thomas J.	7/24/2012-7/23/2014	Not Recv'd
Sambanthamoorthy, Karthik	Wagar, Eric James	3/1/2011-2/28/2015	Not Recv'd
Simonelli, Guido	Balkin, Thomas J.	10/6/2014-10/5/2015	
Tenenbaum, Laura Subbiah	Yourick, Debra Lynn	6/3/2013-6/2/2015	
Zarling, Stasya Nicole	Krzych, Urszula	2/7/2011-2/6/2016	

Table 3: Associates' Activities

- 15 Associates ended tenure during the report period
- 29 months was the average tenure length
- 48 months was the longest
- 7 months was the shortest
- 11 submitted final reports

In the final reports, Associates indicated the following scholarly activity while on tenure.

- **34** Articles published in refereed journals
- 1 Patent applications
- 4 International presentations
- 39 Domestic presentations
- 1 Awards

After ending their tenure, Associates indicated their future plans as follows:

- 1 Permanent position at the NRC host agency
- **6** Contract or temporary position at the NRC host agency
- 2 Research/administrative position with another U.S. government agency
- **0** Research/administrative position with foreign government agency
- 0 Research/teaching at US college/university
- 2 Research/teaching position at a foreign college or university
- **0** Research/administrative position in private industry in the U.S.
- **0** Research/administrative position in private industry outside of the U.S.
- **0** Research/administrative position with a non-profit
- **0** Self-employed/consulting
- O Postdoctoral Research
- 0 Other
- **0** No information provided

In their final reports, Associates were asked to evaluate certain aspects of their experiences on a scale of 1 (low) to 10 (high). The average rating for each item follows:

- 8.2 Short-term value (lab)-Development of knowledge, skills, and research productivity at lab
- 8.6 Long-term value (career)-How your Research Associateship affected your career to date
- 8.6 Laboratory Support-Equipment, funding, orientation, safety & health training, etc.
- 7.4 Adviser Mentoring-Quality of mentoring from the Research Adviser
- 9.5 LPR Support-Quality of administrative support from the LPR
- 9.8 NRC Support-Quality of administrative support from the NRC

Tenure Dates Associate Caudle, Krista 1/28/2013-7/13/2014 Current literature review on preclinical investigations of drug treatments for traumatic brain injury shows that the majority of studies use only a single dose of the experimental drug within ~1 hour of the injury. Longer dosing regimens should be explored further. Three days of twice daily Levetiracetam (Keppra) treatment (50 mg/kg concentration) attenuates nonconvulsive seizures in our model (previous colleague's work), however three days is not sufficient to bring about neurofunctional improvements in motor and cognitive performance (completed dosing duration study). The findings from the dosing duration study establish that a ten day dosing regimen (50 mg/kg) is required for a significant therapeutic benefit in cognitive and motor performance after penetrating severe traumatic brain injury in the rat. Ten days of twice daily Keppra dosing will be used in the full dose response study; dose concentrations to be tested are 12.5 mg/kg, 25 mg/kg, 100 mg/kg, 200 mg/kg, and 800 mg/kg (currently underway). Given our positive results so far, Keppra is a prime target and qualifies for combination drug therapy with Minocycline or other drugs also showing therapeutic benefit in our model, i.e. Simvastatin. Hurtgen, Brady 12/3/2012-9/18/2014 1 Determined Staphylococcus aureus biofilms induced osteoblast necrosis and apoptosis (See publication 1). Showed Dakin's solution reduced macrophage phagocytosis of fungal spores (See publication 2). Determined that osteotomy plus volumetric muscle loss resulted in increased collagen deposition in muscle tissue (See publication #3). Developed a rat model of polytrauma that is relevant to military trauma and characterized the ensuing immune 5 Determined that fracture healing is delayed in the newly developed rat model of polytrauma (In progress). Showed heightened and prolonged innate and adaptive immune responses following complex musculoskeletal injury (osteotomy plus volumetric muscle loss; Manuscript in progress). Determined muscle autograft therapy reduced inflammation, which correlated with improved healing of both bone and muscle tissue following complex musculoskeletal injury (Manuscript in progress). Found that cells isolated from nine different anatomical locations on a pig could be cultured and differentiated into mesenchymal stem cells as determined by increased expression of CD90 and CD105 expression (Work in preparation for a figure in an upcoming manuscript). Identified optimal transfection conditions to knockdown Pax7 gene expression by shRNA in skeletal muscle tissue. Others will perform future studies to knockdown Pax7 following musculoskeletal injury. Krever, Stefan 12/7/2012-5/31/2014 1 Until now only preliminary data of the project exist (see ADVISER/MENTOR SUPPORT) 2 The use of a low-flow CO2 removal device enables to reduce the invasiveness of mechanical ventilation Recirculation of ultrafiltrate does not improve CO2 removal in a low-flow CO2 removal device (see 9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH) Acidification of blood entering a membrane lung can enhance CO2 removal (see 11)PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES) Maes. Piet 12/3/2012-6/2/2014 1 There is no significant difference in genome organization between hantaviruses from a high hantavirus incidence region and a low incidence region 2 Hamsters can be chronically infected with Hantaan virus and Puumala virus 3 Immunosupressed hamsters infected with Puumala virus develop disease 21 dpi Nyland, Jennifer 2/1/2013-12/31/2014 Developed collaborations with the BAMC Pain Management Clinic, focus on translational work from bench to bedside, clinical research involving opioid use and long term outcomes Developed collaborations with the USAISR Burn Center, clinical studies focused on psychological aspects of pain, opioid use, and long term outcomes Testing of novel analgesics in animal models of burn injury 4 Tested the effects of opioid administration during recovery on later drug-seeking behaviors in a rat model 5 Investigated stress as a pain generator, and possible interventions in a rat model 9/4/2012-2/6/2015 Pilia, Marcello 1 Successfully vascularized a Volumetric Muscle Loss defect using Microvascular fragments 2 Proved that increase in vascularization in soft tissue does not increase healing without a myogenic cell source

Contract Technical Report Contract # W81XWH-12-2-0010 Report Period: 05/01/2014-04/30/2015

system

U.S. Army Medical Research & Materiel Command 5/4/2015, 2:55 PM

Successfully vascularized demineralized bone allografts using microvascular fragments both in an ectopic rat model and in a 6mm femoral defect. Again, without an appropriate cell source vascularization is not enough Started investigating the addition of satellite cells and/or minced muscle grafts to the microvascular fragments to determine functional outcome Rahman, Md. Mizanur 3/1/2011-10/5/2014 1 Discovered that the C-terminus of Botulinum neurotoxin serotype A is involved in product removal and catalysis Developed enzymatic assay for BoNT/A catalytic domain Demonstrated that BoNT bound ions affect enzymatic activity Demonstrate that C-terminus of BoNT/A Lc interacts with BoNT/A belt affecting catalysis Sanchez, Carlos 9/7/2011-9/6/2014 Developed in vitrobiofilm assays to test susceptibility to various antimicrobials (and antiseptics) as well as to evaluate the effectiveness of various biofilm dispersal agents utilizing a number of bacterial species as well as fungal isolates related to combat casualties. Reported through prospective studies, the importance and incidence of biofilm formation by clinical isolates associated with combat casualty and showing the relationship between this phenotype and the development of persistent infections in combat related wounds. Demonstrated the utility of combinations of biofilm dispersal agents and antimicrobials as an alternate therapy for targeting bacterial biofilms. Through collaborative efforts contributed to the development of biomaterials capable of delivering biofilm dispersal agents (alone or in combination with antimicrobials) to reduce infection in contaminated femoral segmental defects. Characterized host responses of osteoblasts, a bone cell line, to biofilms vs. planktonic (culture grown) bacteria, and identified those factors responsible for reducing cell viability and cell differentiation. Characterized temporal host responses during bacterial osteomyelitis infection in vivo and have begun o identify factors that may be responsible for host pathologies associated with orthopaedic infections, namely those involving S. aureus. Stonier, Spencer 8/1/2011-6/30/2014 Antibody responses appear to be most acutely responsible for protection against filovirus infection after vaccination CD8 T cells may contribute to protection but it varies by mouse strain slightly 3 Both CD4 and CD8 T cell responses to Ebola glycoprotein are detectable after VRP vaccination Ward, Catherine 8/22/2011-9/4/2014 Utilized and optimized an injectable polyurethane (PUR) matrix for delivery of cells (bone marrow mesenchymal stem cells, BMSCs) and osteogenic agents (Lovastatin, LV) for a bone regeneration therapy in collaboration with Dr. Scott Guelcher (Vanderbilt University). Developed methods to encapsulate cells in alginate matrices for survivability during PUR curing. Analyzed cell fate within injectable scaffolds (PUR). In vitro analysis included determining viability, attachment and proliferation of cells onto the scaffolds in culture. In vivo analysis included determining cell survivability after injection in a rat calvarial defect.

Investigated osteogenic potential of injectable cell delivery scaffolds with the addition of osteogenic agents in the

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) Associate Last or Family Nam	ne	First Name	M.I.			
Caudle		Krista		L.		
2) FORWARDING Address (to w	hich your tax statement will be mailed)	FORWARDIN	IG Phone(s) and E-Mail (if			
Residence or Institution Walter 1 503 Robert Grant Ave.	Reed Army Institute of Research	known) Home Phone: Alt. Phone:				
Silver Spring, MD 20910		Preferred E-ma	ш:			
1 0/		D. CT				
3) Today's Date		Dates of Tenure				
June 15, 2014		from January	28, 2013 to June 13, 2014			
4) Host Agency	Laboratory or Center		Division / Directorate / Departmen	ıt .		
WRAIR	Center for Military Psychiata	ry and	Brain Trauma Neuroprotection	and		
(e.g., AFRL)	Neuroscience		Neurorestoration Branch			
	(e.g., Wright Patterson AFB)		(e.g., High-Speed Propulsion)			
5) Name of Laboratory NRC Advi	iser (and USMA Mentor, if applicable)					
Frank C. Tortella, PhD						

6) TITLE OF RESEARCH PROPOSAL

Combination Drug Therapy for Traumatic Brain Injury: Keppra and Minocycline

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - 1) Current literature review on preclinical investigations of drug treatments for traumatic brain injury shows that the majority of studies use only a single dose of the experimental drug within ~1 hour of the injury. Longer dosing regimens should be explored further.
 - 2) Three days of twice daily Levetiracetam (Keppra) treatment (50 mg/kg concentration) attenuates nonconvulsive seizures in our model (previous colleague's work), however three days is not sufficient to bring about neurofunctional improvements in motor and cognitive performance (completed dosing duration study).
 - 3) The findings from the dosing duration study establish that a ten day dosing regimen (50 mg/kg) is required for a significant therapeutic benefit in cognitive and motor performance after penetrating severe traumatic brain injury in the rat.
 - 4) Ten days of twice daily Keppra dosing will be used in the full dose response study; dose concentrations to be tested are 12.5 mg/kg, 25 mg/kg, 100 mg/kg, 200 mg/kg, and 800 mg/kg (currently underway).
 - 5) Given our positive results so far, Keppra is a prime target and qualifies for combination drug therapy with Minocycline or other drugs also showing therapeutic benefit in our model, i.e. Simvastatin.

(USMA Davies Fellow: please add summary of teaching, including classes taught.) NA

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

I am currently writing the manuscript for the first completed study establishing the optimal dosing duration for Levetiracetam (Keppra). I am in Phase 1A (Year 2) of the proposal currently performing the full dose-response study for Keppra.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

NA

b) Books, book chapters, other publications

NA

c) Manuscripts in preparation, manuscripts submitted

Krista Caudle, Deborah Shear, Andrea Mountney, Kara Schmid, Frank Tortella, Xi-Chun May Lu. Levetiracetam Treatment for Nonconvulsive Seizures and Neuroprotection in a Model of Penetrating Ballistic-Like Brain Injury in the Rat. in preparation for *J. Neurotrauma*

10)	PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.
	NA .
11)	PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.
	International
	NA NA
	Domestic
	Krista Caudle, Deborah Shear, Rebecca Pedersen, Justin Sun, William Flerlage, Julie Faden, Andrea Mountney, Kara Schmid, Frank Tortella, Xi-Chun May Lu (2014). Neuroprotective Effects of Levetiracetam Requires Extended Treatment in a Rat Model of Penetrating Ballistic-like Brain Injury. 32 nd Annual Symposium of the National Neurotrauma Society, San Francisco, CA.
	Krista Caudle, Rebecca Pedersen, Justin Sun, William Flerlage, Julie Faden, Andrea Mountney, Kara Schmid, Deborah Shear, Frank Tortella (2014). Evaluation of Levetiracetam in the WRAIR PBBI Model: Studies from the Operation Brain Trauma Therapy (OBTT) Consortium. 32 nd Annual Symposium of the National Neurotrauma Society, San Francisco, CA.
12)	SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars
	NA
12)	DDAEESSIANA LAWADDS DECENJED DUDING TENUDE
,	PROFESSIONAL AWARDS RECEIVED DURING TENURE
	NA .
14)	POST-TENURE POSITION / JOB TITLE
	Research Biologist DB-03
15)	NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION
	Walter Reed Army Institute of Research, Center for Military Psychiatry and Neuroscience, Brain Trauma Neuroprotection and Neurorestoration Branch, 503 Robert Grant Ave. Silver Spring, MD 20910
	POST-TENURE POSITION STATUS / CATEGORY Please indicate only one. Permanent position at the NRC host agency
exp	(For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DUIRNG TENURE Itemize periences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also mize what you have done to share your culture with your colleagues and the community.
	1) NA
	2)
	3)
	4)
	5)
	APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM 1 a scale of 1 – 10 (poor - excellent), please rate the following:
	SHORT TERM VALUE Development of knowledge, skills, and research productivity

Comments

LONG TERM VALUE

10 How the NRC Associateship award affected your career to date

Comments

LAB SUPPORT

10 Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

ADVISER/MENTOR SUPPORT

10 Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

LPR SUPPORT

Quality of administrative support from the $\underline{\mathbf{L}}$ aboratory (e.g., NIST, NRL, IWR, FHWA) NRC $\underline{\mathbf{P}}$ rogram $\underline{\mathbf{R}}$ epresentative (LPR)

Comments

NRC SUPPORT

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

Asha Davis: adavis@nas.edu
Linda Sligh: Isligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id# Rev. April. 2014 Proj/Act ID#

Research Associateshin Programs

National Research Council	Engineering, and meanine		research rissociateship 110	Siams
	FINAL	REPORT	7	
1) Associate Last or Family Name	•	First Name		M.I.
Haddow		Andrew		D
2) FORWARDING Address (to whi	ich your tax statement will be mailed)	FORWARDIN	IG Phone(s) and E-Mail (if	ļ.
Residence or Institution Street		known) Home Alt. Phone: Preferred E-ma		
3) Today's Date		Dates of Tenus	re	
12 December 2014		from April 20	14 to November 2014	
4) Host Agency	Laboratory or Center		Division / Directorate / Departmen	t
MRMC	USAMRIID		Virology	
(e.g., AFRL)	(e.g., Wright Patterson AF	B)	(e.g., High-Speed Propulsion)	
5) Name of Laboratory NRC Advisor	er (and USMA Mentor, if applicable)			
Michael Turell				
6) TITLE OF RESEARCH PRO 7) SUMMARY OF RESEARCH		ficant findings in	concise form, utilizing key concepts/words.	
1) None				
2)				
3)				
4)				
5) (USMA Davies Fellow: please ad	ld summary of teaching, including cla	sses taught.)		
8) RESEARCH IN PROGRESS None	Describe in no more than 100 word	ls.		

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

None

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

None

10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.

None

11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

None

Domestic

None

12) <i>SEN</i> Nor	MINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars ne
13) <i>PR</i> (Nor	OFESSIONAL AWARDS RECEIVED DURING TENURE ne
•	ST-TENURE POSITION / JOB TITLE search Entomologist
15) <i>NAM</i>	ME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION
Contra	nctor with Ke`aki Technologies
1425 P	I States Army Medical Research Institute of Infectious Diseases Porter Street, Fort Detrick rick, MD, 21702-5011
Perr X Control Abbar Reso gov Reso gov Reso gov	### TT-TENURE POSITION STATUS / CATEGORY Please indicate only one. ### manent position at the NRC host agency Research/administration position in private industry in the U.S. Research/administration position in private industry outside of the U.S. Research/administration position in private industry outside of the U.S. Research/administration position with a non profit Self-employed/consulting Postdoctoral research Other (Please specify, possible) No information provided No information
experie	or J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE Itemize nees that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also what you have done to share your culture with your colleagues and the community.
1)	
2)	
3)	
4)	
5)	
	PRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM cale of 1 – 10 (poor - excellent), please rate the following:
	ORT TERM VALUE Development of knowledge, skills, and research productivity Comments
<u>LC</u>	NONG TERM VALUE How the NRC Associateship award affected your career to date Comments
<u>LA</u>	AB SUPPORT Quality of support from the Laboratoryequipment, funding, orientation, safety and health guidelines, etc. Comments
<u>ΑΓ</u>	OVISER/MENTOR SUPPORT Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable) Comments
<u>LP</u>	PR SUPPORT Quality of administrative support from the <u>L</u> aboratory (e.g., NIST, NRL, IWR, FHWA) NRC <u>P</u> rogram <u>R</u> epresentative (LPR)

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

I still do not have access to the facilities to perform the NRC research project that I was awarded. As such I have been unable to perform any research at USAMRIID.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

Asha Davis: adavis@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id# Rev. September 2014 Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) Associate Last or Family Name			First Name M			
Hurt	gen		Brady			J
2) FO	ORWARDING Address (to w	hich your tax statement will be mailed)	FORWARDIN	G Phone(s) and E-	Mail (if	
Residence or Institution Street		known) Home Phone: Alt. Phone: Preferred E-mail:				
City, S	State Zip		110101100 23 111			
3) <i>Too</i>	day's Date		Dates of Tenur	re		
9-19-	-14		from Decembe	er 3, 2012	to September 18, 2014	
4)	Host Agency	Laboratory or Center		Divisio	n / Directorate / Departmen	t
	AMRMC	AISR		Extremity Tra	auma & Regenerative M	Iedicine
	(e.g., AFRL)	(e.g., Wright Patterson AFB))	(e.g	., High-Speed Propulsion)	
5) <i>Na</i>	me of Laboratory NRC Adv	iser (and USMA Mentor, if applicable)		·		
D	r. Joseph C. Wenke					

6) TITLE OF RESEARCH PROPOSAL

Development and use of a rat model of polytrauma to evaluate therapies that reduce inflammation and restore normal wound healing

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

 Note: These include finding from other research projects that I participated in during my postdoc studies.
 - 1) Determined Staphylococcus aureus biofilms induced osteoblast necrosis and apoptosis (See publication 1).
 - 2) Showed Dakin's solution reduced macrophage phagocytosis of fungal spores (See publication 2).
 - 3) Determined that osteotomy plus volumetric muscle loss resulted in increased collagen deposition in muscle tissue (See publication #3).
 - 4) Developed a rat model of polytrauma that is relevant to military trauma and characterized the ensuing immune response.
 - 5) Determined that fracture healing is delayed in the newly developed rat model of polytrauma (In progress).
 - 6) Showed heightened and prolonged innate and adaptive immune responses following complex musculoskeletal injury (osteotomy plus volumetric muscle loss; *Manuscript in progress*).
 - 7) Determined muscle autograft therapy reduced inflammation, which correlated with improved healing of both bone and muscle tissue following complex musculoskeletal injury (*Manuscript in progress*).
 - 8) Found that cells isolated from nine different anatomical locations on a pig could be cultured and differentiated into mesenchymal stem cells as determined by increased expression of CD90 and CD105 expression (Work in preparation for a figure in an upcoming manuscript).
 - 9) Identified optimal transfection conditions to knockdown *Pax7* gene expression by shRNA in skeletal muscle tissue. Others will perform future studies to knockdown *Pax7* following musculoskeletal injury.

(USMA Davies Fellow: please add summary of teaching, including classes taught.) $N\!A$

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

As I participated in multiple research projects, continuing research will involve the following:

- 1. Confirming polytrauma delays wound healing in the developed rat model (*done by others*) and preparing a manuscript (*done by myself*).
- 2. Analyze data to assess purity of porcine stem cells isolated from nine different anatomical locations. (Figure in a manuscript).
- 3. Continued research in immunomodulation studies of complex musculoskeletal injury. This includes use of drugs and shRNA to target innate and adaptive immune cells as well as shRNA to target satellite cells. (This will be performed by others, but I will participate in data interpretation and manuscript preparation)
- 9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

- Sanchez, C.J., Ward, C.L., Romano, D.R., Hurtgen, B. J., Hardy, S. K., Woodbury, R.L., Trevino, A.L., Rathbone, C.R., and J.C. Wenke. 2013. Staphylococcus aureus biofilms decrease osteoblast viability, inhibits osteogenesis and increases bone resorption in vitro. BMC Musculoskelet Disord. 14:187. Cardile, A. P., Sanchez, C. J., Hardy, S. K., Romano, D.R., Hurtgen, B. J., Wenke, J., Murray, C. K., and K. S. Akers. 2014. Dakin's Solution Alters Macrophage Viability and Function In Vitro. J Surg Res. (Epub ahead of print). Garg, K., Ward, C. L., Hurtgen, B. J., Wilken, J. M., Stinner, D. J., Wenke, J. C., Owens, J., and B. T. Corona. 2014. Volumetric muscle loss: persistent functional deficits beyond frank loss of tissue. J Orthop Res. In Press. b) Books, book chapters, other publications None c) Manuscripts in preparation, manuscripts submitted Hurtgen, B. J., Garg, K., Ward, C. L., B. T. Corona. Concomitant musculoskeletal injury delays fracture healing and alters the immune response. In preparation for PNAS. 10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications. NA 11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location. International None **Domestic** Concomitant Musculoskeletal Injury Results in Delayed Healing and Altered Immune Response. Hurtgen, B. J., Garg, K., Ward, C. L., Wenke, J. C., B. T. Corona. 2nd Annual San Antonio Postdoctoral Research Forum, San Antonio, TX. Submitted abstracts for upcoming conferences: Concomitant Musculoskeletal Injury Results in Delayed Fracture Healing and Heightened and Prolonged Immune Response. Hurtgen, B. J., Garg, K., Ward, C. L., Wenke, J. C., B. T. Corona. Orthopaedic Research Society Annual Meeting, Las Vegas, NV. 12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars, None 13) PROFESSIONAL AWARDS RECEIVED DURING TENURE 1st Place Poster Presentation at the 2nd Annual San Antonio Postdoctoral Research Forum (September 16, 2014) 14) POST-TENURE POSITION / JOB TITLE **Immunologist** 15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION Joint Inflammatory Modulation of Trauma Research Program/ US Air Force 16) POST-TENURE POSITION STATUS / CATEGORY Please indicate only one. Permanent position at the NRC host agency Research/administration position in private industry in the U.S. Contract or temporary position at the NRC host Agency Research/administration position in private industry outside of Abbreviate Host Laboratory/Center
- Other (Please specify, possible) Research/teaching position at a U.S. college or university No information provided Research/teaching position at a foreign college or university 17) (For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also

Research/administration position with a non profit

Self-employed/consulting

Postdoctoral research

Research/Administrative position with another U.S.-

Research/Administrative position with a foreign-

itemize what you have done to share your culture with your colleagues and the community.

government agency

government agency

- 1)
- 2)
- 3)
- 4)
- 5)

18) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM

On a scale of 1 - 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

Development of knowledge, skills, and research productivity **Comments**

LONG TERM VALUE

How the NRC Associateship award affected your career to date

Comments

My training prepared me and allowed me to obtain the position I am moving onto.

LAB SUPPORT
Onestic Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

ADVISER/MENTOR SUPPORT

Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

LPR SUPPORT

Quality of administrative support from the Laboratory (e.g., NIST, NRL, IWR, FHWA) NRC Program Representative (LPR)

Comments

Responsive

U Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

Very pro-active, timely, friendly, and responsive.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Compare your metrics to other Postdoc agencies and see where NRC fits in.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

adavis@nas.edu Asha Davis: Linda Sligh: lsligh@nas.edu Melanie Suydam: msuydam@nas.edu pwilson@nas.edu Peggy Wilson:

Rev. September 2014 Id# Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) Associate Last or Family Name		First Name				
Kreye	r		Stefan		FX	
2) <i>FOR</i>	WARDING Address (to wh	hich your tax statement will be mailed)	FORWARDIN	IG Phone(s) and E-Mail (if known)		
Docidon	ce or Institution V		Home Phone:			
	ce or Institution y		Alt. Phone:			
Street			Preferred E-mail:			
City, Sta	•		D 45			
3) Toda	y's Date		Dates of Tenure			
05/04/2014		from 12/06/2012 to 05/31/2014				
4)	Host Agency	Laboratory or Center		Division / Directorate / Departmen	nt .	
	US Army	ISR		CICR		
	(e.g., AFRL)	(e.g., Wright Patterson AFB)		(e.g., High-Speed Propulsion)		
5) <i>Nam</i>	e of Laboratory NRC Advi	ser (and USMA Mentor, if applicable)				
Mi	chal Dubick	Andriy Batchinsky				

6) TITLE OF RESEARCH PROPOSAL

The effect of spontaneous breathing in combination with extracorporeal lung support in experimental lung injury

Changed to

Early usage of a low flow CO₂ – removal device (hemolung) in acute lung injury

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - 1) Until now only preliminary data of the project exist (see <u>ADVISER/MENTOR_SUPPORT</u>)
 - 2) The use of a low-flow CO₂ removal device enables to reduce the invasiveness of mechanical ventilation
 - 3) Recirculation of ultrafiltrate does not improve CO₂-removal in a low-flow CO₂ removal device (see 9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH)
 - 4) Acidification of blood entering a membrane lung can enhance CO_2 -removal (see 11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

At the moment I am calculating and deriving specific parameters of mechanical ventilation (e.g. tidal volume, minute ventilation, airway pressures). With these parameters I hope I am able to show if the low-flow CO_2 removal device (hemolung) is sufficient to reduce invasiveness of mechanical ventilation.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

- a) Publications in peer-reviewed journals
 - 1) **Title:** Modular Extracorporeal Life Support: effects of ultrafiltrate recirculation on the performance of an extracorporeal carbon dioxide removal (ECCO₂R) device

Authors:

Vittorio Scaravilli, Stefan Kreyer, Katharina Linden, Slava Belenky, Bryan Jordan, Antonio Pesenti, Leopoldo C. Cancio, Andriy I. Batchinsky

2) Title: Extracorporeal blood purification in burns: A review

Authors: Katharina Linden, Ian J. Stewart, Stefan Kreyer, Vittorio Scaravilli, Jeremy W. Cannon, Leopoldo C. Cancio, Andriy I. Batchinsky, Kevin K. Chung

Burns. 2014 Feb 15. pii: S0305-4179(14)00026-6. doi: 10.1016/j.burns.2014.01.013. [Epub ahead of print] Review.

b) Books, book chapters, other publications

c)	Manuscri	pts in	preparation	. manuscript	s submitted

- 1) Title: Extracorporeal CO₂ removal: Effect of short time infusion of three different metabolic acids Authors: Vittorio Scaravilli, Stefan Kreyer, Katharina Linden, Bryan Jordan, Antonio Pesenti, Christian Putensen, Leopoldo C.Cancio, Andriy I. Batchinsky Abstract and Poster presented at SCAI (Society for Complexity in Acute Illness) international meeting. Undergoing submission to ASAIO (American Society for Artificial Internal Organs) journal
- Title: Extracorporeal Membrane Oxygenation and mechanical ventilation Review paper in progress.
- 10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.

none

11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

- Title: Extracorporeal CO₂ removal: Effect of short time infusion of three different metabolic acids
 Authors: Stefan Kreyer, Vittorio Scaravilli, Katharina Linden, Bryan Jordan, Antonio Pesenti, Christian Putensen, Leopoldo C.Cancio, Andriy I. Batchinsky
 Abstract and Poster presented at SCAI (Society for Complexity in Acute Illness) international meeting, Budapest 2013.
- 2) **Title:** Modular Extracorporeal Life Support: effects of ultrafiltrate recirculation on the performance of an extracorporeal carbon dioxide removal (ECCO₂R) device

Authors:

Vittorio Scaravilli, Stefan Kreyer, Katharina Linden, Slava Belenky, Bryan Jordan, Antonio Pesenti, Leopoldo C. Cancio, Andriy I. Batchinsky

Abstract and Poster presented at SCAI (Society for Complexity in Acute Illness) international meeting, Budapest 2013.

Domestic

none

none

- 12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars.
- 13) PROFESSIONAL AWARDS RECEIVED DURING TENURE

none

14) POST-TENURE POSITION / JOB TITLE

Anesthesiologist at the University hospital of Bonn, Germany

15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION

University hospital Bonn, Dept. for Anesthesiology and operative Intensive Care medicine, Sigmund-Freud-Str 25, 53127 Bonn, Germany

16)	POST-TENURE POSITION STATUS / CATEGORY Please indicate	only	y one.
	Permanent position at the NRC host agency		Research/administration position in private industry in the U.S.
	Contract or temporary position at the NRC host Agency		Research/administration position in private industry outside of
	Abbreviate Host Laboratory/Center		the U.S.
	Research/Administrative position with another U.S		Research/administration position with a non profit
	government agency		Self-employed/consulting
	Research/Administrative position with a foreign-		Postdoctoral research
	government agency		Other (Please specify, possible)
	Research/teaching position at a U.S. college or university		No information provided
X	Research/teaching position at a foreign college or university	_	1

17) (For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DUIRNG TENURE Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

- Everyone in the lab, co-researchers as well as technicians helped me getting to know a lot about American culture, ways of thinking and traditions. During lunchtime often political issues where discussed so that I got the possibility to understand the opinions of different people living in the USA. My colleagues took me to local events like Rodeo and Fiesta. They invited me to share American Holidays with them, like Thanksgiving, so that I had the possibility to experience traditions along with culinary specialties. Whenever I had questions regarding culture but also things concerning daily life in the USA everyone was always offering help.
- 2) In a lot of discussions regarding political issues and way of life I was able to offer a foreigner's perspective on things. I invited my colleagues to get to know German food. Interestingly, the part of Texas where I stayed was already influenced by German culture and I was able to tell my colleagues what of this was "real German" and what more American.

3)

4)

5)

18) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM

On a scale of 1 - 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

7 Development of knowledge, skills, and research productivity

Comments

The program gave me the possibility to learn and improve my skills in animal research. I improved my skills in scientific writing by the review of co-workers and supervisors.

LONG TERM VALUE

How the NRC Associateship award affected your career to date

Comments

At this point, the NRC award did not influence my career very much. I think that this will change in the future if scientific papers will result out of my work. Furthermore, the experience of working in another country, together with improvements in the English language, will enable me to plan and structure my research better in the future.

<u>LAB SUPPORT</u>

Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc.

Comments

The equipment of this laboratory was extraordinary and the possibilities that this laboratory could have offered are extremely good. In my opinion these incredible possibilities could not be used to full extent. The laboratory personnel were helpful and tried to fulfill the tasks that were given. This was sometimes complicated by a big workload on them due to simultaneously ongoing projects and the fact that research goals and working plans were not communicated in this lab, which I felt let to a certain frustration. The ISR has strict regulations about health guidelines and training before entering the laboratory. Although these regulations reduced the effectiveness of the laboratory and led to a delayed start of the experiments, I appreciate the required training in the beginning.

ADVISER/MENTOR SUPPORT

Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

After I finished all the ISR specific requirements like training and in-processing, I was told that grants for the project I planned were canceled, so that I could not perform the study I applied with. This was especially disappointing because I started to prepare a smaller side-project to the original planned study here. After investing effort into the main- and the side-project it was very frustrating that this work was done for nothing. After speaking with my adviser and explaining my frustration the relationship got tense. Finally I was offered to work on another project that was already planned and funded. I did not have the possibility to influence this project like I would have liked to do and it did not exactly meet my goals for coming to this laboratory, but will hopefully lead to a publication in the end. I think that the communication about the planned projects and the goals of the laboratory was suboptimal. The changed project also led to a late start of experiments which results in the fact that I cannot finish my work while being in the USA.

Regarding my family situation (e.g. I became a father while being in the USA) my mentor was always understanding and offered help and support.

LPR SUPPORT

Quality of administrative support from the <u>L</u>aboratory (e.g., NIST, NRL, IWR, FHWA) NRC <u>P</u>rogram <u>R</u>epresentative (LPR) Comments

Whenever I needed help, Dr. Dubick was able to help me. Also contacting him was very easy. I had no need to contact him very often, therefore I can't go into further details.

NRC SUPPORT

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

I was very impressed and satisfied with the help and support by NRC. Thank you very much.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

Asha Davis: adavis@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu



Id# Rev. April. 2014 Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) Associate Last or Family Nan	ne	First Name	M.I.	
Maes		Piet		
2) FORWARDING Address (to w	hich your tax statement will be mailed)	FORWARDIN	G Phone(s) and E-Mail (if	
Residence or Institution Residence		known) Home Phone: Alt. Phone:		
Street		Preferred E-ma	ail:	
City, State Zip				
3) Today's Date		Dates of Tenur	re	
29 MAY 2014		from 1 DEC 2	012 to 31 MAY 2014	
4) Host Agency	Laboratory or Center		Division / Directorate / Departme	ent
USAMRIID	Molecular Virology		Virology	
(e.g., AFRL)	(e.g., Wright Patterson AFB)		(e.g., High-Speed Propulsion)	
5) Name of Laboratory NRC Adv	iser (and USMA Mentor, if applicable)			
dr. Jay HOOPER				

6) TITLE OF RESEARCH PROPOSAL

Manipulating the Syrian hamster model for use in developing medical countermeasures to HFRS

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - 1) There is no significant difference in genome organization between hantaviruses from a high hantavirus incidence region and a low incidence region
 - 2) Hamsters can be chronically infected with Hantaan virus and Puumala virus
 - 3) Immunosupressed hamsters infected with Puumala virus develop disease 21 dpi

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

Both hamster models (i.e. *Hantaan virus* and *Puumala virus* disease models) need to be further refined to show that the disease observed is specifically caused by the infection with *Hantaan virus* or *Puumala virus*. Furthermore, it is important to minimize the immunosuppression therapy for the hamsters. Additional experiments need to be performed to examine which level of immune suppression needs to be reached to develop disease in the hamsters.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

none

b) Books, book chapters, other publications

none

c) Manuscripts in preparation, manuscripts submitted

none

10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.

none

11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

none

	Domestic none
12	2) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminar 'Zoonotic viruses in Belgian wildlife'. September 25, 2013. Pasteur Institute, Brussels, Belgium
13	s) PROFESSIONAL AWARDS RECEIVED DURING TENURE
	none
14) POST-TENURE POSITION / JOB TITLE
	Research leader at the Zoonotic Infectious Diseases Unit
15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION
	KU Leuven, Rega Institute, Minderbroedersstraat 10, BE3000 Leuven Belgium.
	POST-TENURE POSITION STATUS / CATEGORY Please indicate only one. Permanent position at the NRC host agency Research/administration position in private industry in the U.S. Contract or temporary position at the NRC host Agency Research/administration position in private industry outside of the U.S. Research/Administrative position with another U.S. Research/administration position with a non profit government agency Self-employed/consulting Postdoctoral research Other (Please specify, possible) No information provided No inform
ex	(For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DUIRNG TENURE Itemize periences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also emize what you have done to share your culture with your colleagues and the community. 1) I had the honor to enjoy the tradition of Thanksgiving twice with colleagues and had a lot of 'American style BBQs' in the Summer.
	2) We had several 'cook-off' occasions in the lab with typical American and Belgian recipes.
	3) For Belgians, it's all about foods and drinks. So we shared a lot of recipes for making typical Belgian foods and desserts. A real Belgian waffle for example, seems to be something completely different than what people are used to.
	4) As a Belgian, I like to talk about politics. It has been very educational knowing about how politics work in the states. It has been very interesting to witness the election of an American president and to go and watch the inauguration speech in D.C.
	5) I tried to educate people here that Belgium is more than just about chocolate, beers and waffles.
) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM on a scale of 1 – 10 (poor - excellent), please rate the following:
	SHORT TERM VALUE Development of knowledge, skills, and research productivity Comments
	LONG TERM VALUE How the NRC Associateship award affected your career to date Comments
	LAB SUPPORT Quality of support from the Laboratoryequipment, funding, orientation, safety and health guidelines, etc. Comments
	ADVISER/MENTOR SUPPORT Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable) Comments
	<u>LPR SUPPORT</u> Quality of administrative support from the <u>L</u> aboratory (e.g., NIST, NRL, IWR, FHWA) NRC <u>P</u> rogram <u>R</u> epresentative (LPR)

Comments

NRC SUPPORT

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

Asha Davis: adavis@nas.edu
Linda Sligh: Isligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id# Rev. April. 2014 Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) <i>Ass</i>	sociate Last or Family Nan	ne	First Name		M.I.
Nylai	nd		Jennifer		E
2) FO	RWARDING Address (to w	hich your tax statement will be mailed)	FORWARDIN	G Phone(s) and E-Mail (if	
Residence or Institution Street		known) Home Phone: Alt. Phone: Preferred E-mail:			
City, S	State Zip				
3) <i>Too</i>	lay's Date		Dates of Tenure		
Dece	mber 19, 2014		from February 1, 2013 to December 31, 2014		014
4)	Host Agency	Laboratory or Center		Division / Directorate / Depart	ment
	AMRMC	USAISR		Pain Management	
	(e.g., AFRL)	(e.g., Wright Patterson AFB)		(e.g., High-Speed Propulsion)
5) Nai	me of Laboratory NRC Adv	iser (and USMA Mentor, if applicable)			
Jo	ohn Clifford				

6) TITLE OF RESEARCH PROPOSAL

The Use of Glial Inhibitors to Increase the Efficacy of Opioid Analgesics while Eliminating the Propensity for Addiction

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - 1) Developed collaborations with the BAMC Pain Management Clinic, focus on translational work from bench to bedside, clinical research involving opioid use and long term outcomes
 - 2) Developed collaborations with the USAISR Burn Center, clinical studies focused on psychological aspects of pain, opioid use, and long tem outcomes
 - 3) Testing of novel analgesics in animal models of burn injury
 - 4) Tested the effects of opioid administration during recovery on later drug-seeking behaviors in a rat model
- 5) Investigated stress as a pain generator, and possible interventions in a rat model (USMA Davies Fellow: please add summary of teaching, including classes taught.)
- 8) RESEARCH IN PROGRESS Describe in no more than 100 words.

All projects during tenure are currently in progress. I will continue to pursue this research in my new position.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

- a) Publications in peer-reviewed journals
 - Clifford, J.L., Fowler, M., Hansen, J.J., Cheppudira, B., Nyland, J.E., Salas, M.M., McGhee, L.L., Petz, L.N. & Loyd, D.R. (2014). Advances in treating pain in wounded service members: A decade at war. Journal of Trauma and Acute Care Surgery, 77(3), S228-S236.
- b) Books, book chapters, other publications
- c) Manuscripts in preparation, manuscripts submitted
 - Nyland, J.E., McLean, S.A. & Averitt, D.R. (Submitted). Sub-chronic stress prior to injury intensifies pain associated with thermal burn injury. Journal of Pain.
 - Nyland, J.E., Escolas, S.M., Aden, J.K., Young, A.W., Chung, K.K. (In Preparation). Preparing for Disaster: Analgesic Needs for Mass Burn Casualties.
 - Linnstaedt, S.D., Riker, K.D., Nyland, J.E., Velilla, M.A., Pearson, C., O'Neil, B.J., Zimny, E., Lewandowski, C., Hendry, P.L., Barnes, S., Rosenberg, M., McLean, S.A. (In Preparation). microRNA 320a is a potential mediator of chronic widespread hyperalgesia development after stress exposure.

Nyland, J.E., Hoang, H.T., Alphonso, C., Guthmiller, K.B., Wilroy, G., Overbaugh, R., Ibarra, A., Goff, B.J., (In Preparation). A Viable Technique: Cervical Medial Branch Blocks in the Sitting Position

10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.

11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Nyland, J.E., McLean, S.A., Clifford, J.L., Fowler, M., Petz, L.N. & Loyd, D.R. (2014). Prior Stress Exposure Increases Pain Behaviors in a Rat Model of Full Thickness Thermal Injury. Abstract for poster presentation, International Association for the Study of Pain World Congress, Buenos Aires, Argentina.

Domestic

Linnstaedt S.D., Riker K.D., Nyland J.E., Velilla M.A., Pearson C., O'Neil B.J., Zimny E., Lewandowski C., Hendry P.L., Barnes S., Rosenberg M. & McLean S.A. (2015). microRNA 320a is a potential mediator of chronic widespread hyperalgesia development after stress exposure. Abstract for the American Pain Society 34th Annual Meeting, Palm Springs, California.

Nyland, J.E., Mclean, S.A. & Averitt, D.L. (2015). Combined serotonin and norepinephrine reuptake inhibition reduces the effects of stress on post-injury pain behaviors in a rat model of burn injury. Abstract for the American Pain Society 34th Annual Meeting, Palm Springs, California.

Nyland, J.E., Escolas, S.M., Rauschendorfer, C.A., Aden, J.K., Young, A.W. & Chung, K.K. (2015). Preparing for disaster: analgesic needs for mass burn casualties. Abstract for the American Pain Society 34th Annual Meeting, Palm Springs, California.

Escolas, S.M., Rauschendorfer, C.A., Walker, S.L., Aden, J.K., Nyland, J.E. & Chung, K.K. (2015). Secure attachment associated with less pain in burn patients. Abstract for the American Burn Association 47th Annual Meeting, Chicago, Illinois.

Fowler, M., Hansen, J.J., Nyland, J.E., Gibbons, R.V. & McGhee, L. (2015). The relationships between opioids and intraoperative fluid administration in a burn operating room. Abstract for the American Academy of Pain Medicine's 31st Annual Meeting, National Harbor, Maryland.

Nyland, J.E., McLean, S.A., Clifford, J.L., Fowler, M., Petz, L.N. & Loyd, D.R. (2014). Prior Stress Exposure Increases Pain Behaviors in a Rat Model of Full Thickness Thermal Injury. Abstract for poster presentation, Military Health Systems Research Symposium, Fort Lauderdale, Florida.

Nyland, J.E., Garza, T.H., Slater, T.M., Clifford, J.L., Fowler, M., Eidson, L.N., Murphy, A.Z. & Averitt, D.L. (2013). Neurobiological mechanisms of tolerance-independent attenuation of morphine efficacy in a rat model of thermal injury. Abstract for oral breakout presentation, Military Health Systems Research Symposium, Fort Lauderdale, Florida.

Nyland, J.E., Garza, T.H., Slater, T.M., Fowler, M., Clifford, J.L., Petz, L.N., & Loyd, D.R. (2013). Development of opioid tolerance in a rat model of full thickness thermal injury. Abstract for poster presentation, Society for Neuroscience, San Diego, California.

Nyland, J.E., Garza, T.H., Slater, T.M., Clifford, J.L., Fowler, M., Eidson, L.N., Murphy, A.Z. & Averitt, D.L. (2013). Neurobiological mechanisms of tolerance-independent attenuation of morphine efficacy in a rat model of thermal injury. Abstract for oral breakout presentation, Military Health Systems Research Symposium, Fort Lauderdale, Florida.

12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars. Substance Use in the Military, USAISR Seminar Series, August 13, 2014

Pain Meds for Algernon: What we can and cannot learn from animal models, USAISR Burns and Trauma Research Workgroup meeting, July 10, 2014

13) PROFESSIONAL AWARDS RECEIVED DURING TENURE

Staff Scientist

15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION

Battlefield Pain Management Task Area, US Army Institute of Surgical Research, 3698 Chambers Pass, Fort Sam Houston, TX 78234 16) POST-TENURE POSITION STATUS / CATEGORY Please indicate only one. Permanent position at the NRC host agency Research/administration position in private industry in the U.S. Contract or temporary position at the NRC host Agency Research/administration position in private industry outside of Abbreviate Host Laboratory/Center <u>USAISR</u> Research/Administrative position with another U.S.-Research/administration position with a non profit government agency Self-employed/consulting Research/Administrative position with a foreign-Postdoctoral research government agency Other (Please specify, possible) Research/teaching position at a U.S. college or university No information provided Research/teaching position at a foreign college or university 17) (For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community. 1) 2) 3) 4) 5) 18) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM On a scale of 1 - 10 (poor - excellent), please rate the following: SHORT TERM VALUE Development of knowledge, skills, and research productivity Comments LONG TERM VALUE How the NRC Associateship award affected your career to date **Comments** LAB SUPPORT Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc. **Comments** ADVISER/MENTOR SUPPORT Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable) **Comments** While I did not receive much support from John Clifford, I did not require much mentorship. Quality of administrative support from the Laboratory (e.g., NIST, NRL, IWR, FHWA) NRC Program Representative (LPR) **Comments**

NRC SUPPORT

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned

signature file below:

Melanie Suyd

Linda Sligh:lsligh@nas.eduAsha Soutar:asoutar@nas.eduMelanie Suydam:msuydam@nas.eduPeggy Wilson:pwilson@nas.edu

Id# Rev. December 2014 Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) <i>Ass</i>	sociate Last or Family Nan	ne	First Name		M.I.
Pilia			Marcello		
2) <i>FO</i>	RWARDING Address (to w	hich your tax statement will be mailed)	FORWARDIN	IG Phone(s) and E-Mail (if	
	ence or Institution		known) Home Phone: Alt. Phone:		
Street			Preferred E-m	ail:	
City, S	State Zip				
3) <i>Too</i>	day's Date		Dates of Tenu	re	
January 29, 2015		from September 4, 2012 to February 6, 2015			
4)	Host Agency	Laboratory or Center		Division / Directorate / Departmen	nt .
	AMRMC	USAISR		ETRM	
	(e.g., AFRL)	(e.g., Wright Patterson AFB)	ı	(e.g., High-Speed Propulsion)	
5) <i>Nat</i>	me of Laboratory NRC Advi	iser (and USMA Mentor, if applicable)			
S	oft Tissue Regeneration	Lab Christopher	Rathbone		

6) TITLE OF RESEARCH PROPOSAL

Composite pre-vascularized scaffolds for large bony defect reconstruction

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - 1) Successfully vascularized a Volumetric Muscle Loss defect using Microvascular Fragments
 - 2) Proved that increase in vascularization in soft tissue does not increase healing without a myogenic cell source
 - 3) Successfully vascularized demineralized bone allografts using Microvascular Fragments both in an ectopic rat model and in a 6mm femoral defect.
 - 4) Again, without an appropriate cell source vascularization is not enough
 - 5) Started investigating the addition of satellite cells and/or minced muscle grafts to the microvascular fragments to determine functional outcome
- (USMA Davies Fellow: please add summary of teaching, including classes taught.)
- 8) RESEARCH IN PROGRESS Describe in no more than 100 words.

Every project was finished and the manuscripts are being published right now. Started investigating addition of myogenic source to microvascular fragments but another PI will assess the outcome in 8 weeks

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

- a) Publications in peer-reviewed journals
 - 1. Pilia M, McDaniel JS, Guda T, Chen XK, Rhoads RP, Allen RE, Corona BT, and Rathbone CR. Transplantation and perfusion of microvascular fragments in a rodent model of volumetric muscle loss injury. European Cell and Material; 28:11-14; 2014
 - 2. McDaniel J, Pilia M, Ward CL, Pollot B, Rathbone CR. Characterization and multilineage potential of cells derived from isolated microvascular fragments. Journal of Surgical Research; E-Pub May 2014
- b) Books, book chapters, other publications
 - 1. Rathbone CR, McDaniel JS, Pilia M. Chapter 9. Cell Sources for Orthopaedic Defects. Biomaterials of Bone Grafts Bench-top to Clinical Applications. Taylor & Francis Group. (In preparation).
- c) Manuscripts in preparation, manuscripts submitted
 - 1. Pilia M, McDaniel JS, Rathbone CR. Prevascularization of demineralized freeze-dried bone allograft in an ectopic model and its effect on segmental bone healing. Journal of Bone and Mineral Research Part A; In preparation; planned submission February 2014

- 2. McDaniel JS, Pilia M, Raut V, Ledford J, Shiels SM, Wenke JC, Barnes BR, Rathbone CR. Currently available alternatives to autograft evaluated in a rabbit segmental bone defect. International Orthopedics; Submitted, January 2015
- 3. McDaniel JS, Pilia M, Hurtgen B, Belenkiy S, Necsoiu C, Batchinsky A, Rathbone CR. Porcine bone marrow aspirate characterization for the support of large animal studies. Research in Veterinary Science; In preparation, expected submission February 2015.
- 4. Walker JA, Pilia M, McDaniel JS, Wenke JC, Rathbone CR; Perfusion CT for Assessment of en bloc Implant Vascular Success. Journal of Vascular Surgery; In preparation; planned submission February 2015sadf
- 10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.
- 11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

- Pilia M*, McDaniel JS, Corona BT, Rathbone CR. Microvascular fragments improve vessel density of allograft bone in vivo; San Antonio Postdoc Research Forum, San Antonio TX, September 2014 Poster Presentation
- 2 McDaniel JS, Pilia M*, Walker J, Corona BT, Rathbone CR. Use of microvascular fragments for improving regeneration in musculoskeletal defects; San Antonio Postdoc Research Forum, San Antonio TX, September 2014 Poster Presentation
- 3 Pilia M*, McDaniel JS, Corona BT, Rathbone CR. Microvascular fragments improve vessel density of allograft bone in vivo; Military Health System Research Symposium, Ft. Lauderdale FL, August 2014 Poster Presentation
- 4 McDaniel JS, Pilia M*, Walker J, Corona BT, Rathbone CR. Use of microvascular fragments for improving regeneration in musculoskeletal defects; Military Health System Research Symposium, Ft. Lauderdale FL, August 2014 Poster Presentation
- 5 Rathbone CR*, Pilia M, McDaniel JS, Corona BT. Transplantation of Microvascular Fragments for Volumetric Muscle Loss; RegenMed SA, February 2014 Oral Presentation 1 Pilia M*, McDaniel JS, Corona BT, Rathbone CR. Transplantation of Microvascular Fragments in an Experimental Volumetric Muscle Loss Model; Tissue Engineering and Regenerative Medicine International Society, Atlanta GA, November 2013 Oral Presentation
- 6 Walker JA*, Pilia M, Walters TJ, McDaniel JS, Wenke JC, Rathbone CR. Perfusion CT for Assessment of en bloc Implant Vascular Success; Tissue Engineering and Regenerative Medicine International Society, Atlant GA, November 2013 Poster Presentation
- 7 Pilia M*, McDaniel JS, Corona BT, Rathbone CR. Transplantation and Perfusion of Microvascular Constructs in an Experimental Volumetric Muscle Loss Model; Military Health System Research Symposium, Ft. Lauderdale FL, August 2013 Oral Presentation
- 8 Pilia M*, McDaniel JS, Corona BT, Rathbone CR. Transplantation and Perfusion of Microvascular Constructs in an Experimental Volumetric Muscle Loss Model; Military Health System Research Symposium, Ft. Lauderdale FL, August 2013 Poster Presentation
- 12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars.
- 13) PROFESSIONAL AWARDS RECEIVED DURING TENURE
- 14) POST-TENURE POSITION / JOB TITLE

Special Assistant, Intra- & Extramural Research Prog.

20874 16) POST-TENURE POSITION STATUS / CATEGORY Please indicate only one. Permanent position at the NRC host agency Research/administration position in private industry in the U.S. Contract or temporary position at the NRC host Agency Research/administration position in private industry outside of Abbreviate Host Laboratory/Center _ Research/Administrative position with another U.S.-Research/administration position with a non profit government agency Self-employed/consulting Research/Administrative position with a foreign-Postdoctoral research government agency Other (Please specify, possible) Research/teaching position at a U.S. college or university No information provided Research/teaching position at a foreign college or university 17) (For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community. 1) 2) 3) 4) 5) 18) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM On a scale of 1 - 10 (poor - excellent), please rate the following: SHORT TERM VALUE Development of knowledge, skills, and research productivity **Comments** LONG TERM VALUE How the NRC Associateship award affected your career to date **Comments** LAB SUPPORT Quality of support from the Laboratory-equipment, funding, orientation, safety and health guidelines, etc. Comments ADVISER/MENTOR SUPPORT Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable) **Comments** LPR SUPPORT Quality of administrative support from the <u>L</u>aboratory (e.g., NIST, NRL, IWR, FHWA) NRC <u>Program Representative</u> (LPR) **Comments** Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.) **Comments** Special thanks to Peggy and Jason for making our lives so much easier. I really want to thank the entire institution, it has been an amazing experience. Thank you!

Combat Casualty Care, Fort Detrick, MD - Job through Capitol IT Solutions, 13907 Carlson Farm Drive, Germantown, MD

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

Linda Sligh: lsligh@nas.edu

Asha Soutar: asoutar@nas.edu

Melanie Suydam: msuydam@nas.edu

Peggy Wilson: pwilson@nas.edu

Id# Rev. December 2014 Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) Asso	ociate Last or Famil	y Name	First Name		M.I.
RAHMAN			Md. Mizanur		
2) <i>FOR</i>	RWARDING Address	s (to which your tax statement will be mailed)	FORWARDING	G Phone(s) and E-Mail (if	
Residence or Institution Street City, State Zip		known) Home Phone: : Alt. Phone: Preferred E-mail:			
3) Toda	ıy's Date		Dates of Tenur	e	
10/01/2	01/2014 from 03/01/2011 to 11/30/2014		1 to 11/30/2014		
4)	Host Agency	Laboratory or Center		Division / Directorate / Department	t
	AMRMC	USAMRIID		MTS	
(e.g., AFRL) (e.g., Wright Patterson AFB)		B) (e.g., High-Speed Propulsion)			
5) <i>Nam</i>	e of Laboratory NR	C Adviser (and USMA Mentor, if applicable)			
Bio	ochemistry	Dr. S. Ashraf Ahmed			

6) TITLE OF RESEARCH PROPOSAL

Effects of Botulinum neurotoxin derived peptides and post-translational modification on the structure, function and biology of BoNT

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - 1) Discovered that the C-terminus of Botulinum neurotoxin serotype A is involved in product removal and catalysis
 - 2) Developed enzymatic assay for BoNT/A catalytic domain
 - 3) Demonstrated that BoNT bound ions affect enzymatic activity
 - 4) Demonstrate that C-terminus of BoNT/A Lc interacts with BoNT/A belt affecting catalysis

5)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

I have been working on to determine the extended role of C-terminus of BoNT/A Lc on the stability and catalytic activity of the enzyme.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

- a) Publications in peer-reviewed journals
- **1. Rahman M Mizanur**, Robert Stafford, and S. Ashraf Ahmed. Cleavage of SNAP25 and its shorter version by the protease domain of serotype A Botulinum neurotoxin. *PLoS One*, 9(4):e95188, **2014**.
- **2. Rahman M Mizanur**, Verna Frasca, Subramanyam Swaminathan, Sina Bavari, Robert G. Webb, Leonard A. Smith and S. Ashraf Ahmed. C-Terminal region of the catalytic domain of type A botulinum neurotoxin stimulate catalysis by facilitating product release. *J. Biol. Chem.* 288, 24223-24233, **2013.**
- **3.** Rahman M. Mizanur, John Gorbet, Subramanyam Swaminathan, and S. Ashraf Ahmed. Inhibition of catalytic activities of botulinum neurotoxin protease domains of serotypes A, B and E by acetate, sulfate and calcium. *Int. J. Biochem. Mol. Biol.* 3, 313-21, **2012.**
- b) Books, book chapters, other publications
- c) Manuscripts in preparation, manuscripts submitted
- 1. **Rahman M. Mizanur**, and S. Ashraf Ahmed ¹The Belt Sequence Mimics the Role of Substrate SNAP25 Upstream Sequence in the Catalysis of type A Botulinum Neurotoxin

2. Vicki A. Montgomery S. Ashraf Ahmed, Mark A. Olson, Rahman M Mizanur , Virginia I. Roxas-Du Leonard A. Smith: <i>Ex vivo</i> inhibition of <i>C. botulinum</i> neurotoxins types B, C, E, and F by Small Mole Weight Inhibitors (Manuscript prepared for Toxicon)	
10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.	
11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location. International	
 May 2013: The C-Terminus of the Catalytic Domain of Type A Botulinum Neurotoxin May Facilitate Production From the Active Site, NIH, Frederick, Maryland September 2012: Roles of Acetate, Sulfate and Calcium on the Catalytic Activities of Botulinum Neurotoxin I Domains of Serotypes A, B and E. IBRCC, Baltimore, Maryland 	
12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and location 1. March 2013: Botulinum Neurotoxin: Structure and Mechanism of Action, University of Maryland, Col	
2. May 2014: Botulinum Neurotoxin: Structure and Mechanism of Action, University of Maryland, College 13) PROFESSIONAL AWARDS RECEIVED DURING TENURE	
14) POST-TENURE POSITION / JOB TITLE Microbiologist 15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION VISUAL STANDARD 1405 Day of the Standard Position / Job Organization	
USAMRIID, 1425 Porter St, Fort Detrick, Frederick 16) POST-TENURE POSITION STATUS / CATEGORY Please indicate only one. X Permanent position at the NRC host agency Research/administration position in private industry Abbreviate Host Laboratory/Center the U.S. Research/Administrative position with another U.S. Research/Administrative position with a foreign-government agency Self-employed/consulting Postdoctoral research government agency Other (Please specify, possible) Postdoctoral provided Research/teaching position at a foreign college or university Research/teaching position at a foreign college or university	ry outside of
17) (For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DURING TENURE Ite experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culturates what you have done to share your culture with your colleagues and the community.	
1)	
2)	
3)	
4) 5)	
18) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM	
On a scale of 1 – 10 (poor - excellent), please rate the following: SHORT TERM VALUE	

Development of knowledge, skills, and research productivity

Comments Excellent (10) LONG TERM VALUE How the NRC Associateship award affected your career to date **Comments** Excellent (10) LAB SUPPORT Quality of support from the Laboratory--equipment, funding, orientation, safety and health guidelines, etc. **Comments** Excellent (10) ADVISER/MENTOR SUPPORT Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable) **Comments** Excellent (10) LPR SUPPORT Quality of administrative support from the Laboratory (e.g., NIST, NRL, IWR, FHWA) NRC Program Representative (LPR) **Comments** Excellent (10)

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

NRC SUPPORT

Excellent (10)

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

Asha Davis: adavis@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id# Rev. September 2014 Proj/Act ID#

Advisers to the Nation on Sdence, Engineering, and Medirine National Research Council

Research Associateship Programs

FINAL REPORT

I)Associate Last or Family Name		First Name		M.I.	
Sanchez Jr		Carlos		J	
2) FORWARDING Address (to which	ch your tax statement will be mailed)	FOR WARDIN	G Phone(s) and E-Mail (if known)		
Residence or Institution		Home Phone:			
Street Ci1y, State Zip		Alt. Phone: Preferred E-m	nail:		
3) Today's Date		Dates of Tenur			
26 August 2014		from 07 Se	pt 2011 to 06 Sept 2014		
4) Host Agency	Laboratory or Center		Division I Directorate I Depart men	t	
ARMC	US Army Institute of Surgica 1	Resea rch,	Combat Casualty Care!Extrem ity Trail	ıma and	
(e.g., AFRL)	JBSA San Anton io TX		Regenera tive Medicine		
1e.I!., Wriglll Parterson AFBI			le.I!.• llieh-Snced Prooulsionl		
5)Name of Laboratory NRCAdviser ((and USMA Mentor, if applicable)	-			

6) TITLE OF RESEARCH PROPOSAL

Joseph C Wenke, PhD

Improving Outcomes of Extremity Trauma through Infection Control and Bone Regeneration

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - I) Developed *in vitro* biofilm assays to test susceptibility to various antimicrobials (and antiseptics) as well as to evaluate the effectiveness of various biofilm dispersal agents utilizing a number of bacterial species as well as fungal isolates related to combat casualties
 - 2) Reported through prospective studies, the importance and incidence of biofilm formation by clinical isolates associated with combat casualty and showing the relationship between this phenotype and the development of persistent infections in combat related wounds
 - 3) Demonstrated the utility of combinations of biofilm dispersal agents and antimicrobials as an alternative therapy for targeting bacterial biofilms
 - 4) Through collaborative efforts contributed to the development of biomaterials capable of delivering biofilm dispersal agents (alone or in combination with antimicrobials) to reduce infection in contaminated femoral segmental defects
 - 5) Characterized host responses of osteoblasts, a bone cell line, to biofilms vs planktonic (culture grown) bacteria, and identified those factors responsible for reducing cell via bility and cell differentiation
 - 6) Characterized temporal host responses during bacterial osteomyelitis infection in vivo and have begun to identify factors that may be responsible for host pathologies associated with orthopaedic infections, namely those involving *S. aureus*

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

The primary focus of my research has been to develop and/or optimize treatment strategies to reduce infectious complications associated with open fractures, sustained during combat trauma. Based on previous work completed at ISR, we have identified a number of currently FDA approved antimicrobials, as well as novel agents capable of specifically targeting and disrupting biofilms, that have shown great efficacy as a treatment option for a number of microbial agents predominately responsible for infection in combat related injuries; moreover which have also been shown to specifically target/disrupt microbial biofilms. We are currently in the process of translating these findings into potential therapies to reduce infection using an established contaminated segmental defect model. Additionally we are testing the application of various materials, loaded with idea agents, to evaluate sustained release of single and multiple compounds

9) PUBLI CATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

Sanchez CJ, Mende K, Beckius ML, Akers KS, Romano DR, Wenke JC, Murray CK. (2013). *Bigftlm formation by clinical isolates and the implications in chronic infections*. BMC Infect Dis. Jan 29; 13:47. doi: 10.1186/1471-2334-13-47.

Sanchez CJ, Ward CL, Romano DR, Hurtgen BJ, Hardy SK, Woodbury RL, Trevino AV, Rathbone CR, Wenke JC. (2013). Staphylococcus aureus biofilms decrease osteoblast viability, inhibits osteogenic differentiation, and increases bone resorption in vitro. BMC Musculoskeletal Disorders. 14:187

<u>Sanchez CJ</u>, Prieto EM, Krueger CA, Zienkiewicz KJ, Romano DR, Ward CL, Akers KS, Guelcher SA, Wenke JC. (2013). *Effects of local delivery of d-amino acids from biofilm-dispersive scaffolds on infection in contaminated rat segmental defects. Biomaterials*. Jul 4. doi:pii: S0142-9612(13)00712-6.

Barsoumian A, Sanchez CJ, Mende K, Tully CC, Beckius ML, Akers KS, Wenke JC, Murray CK. (2013). *In Vitro Toxicity and Activity of Dakin's Solution, Mafenide Acetate, and Amphotericin B on Filamentous Fungi and Human Cells.* J Orthop Trauma. 2013 Jan 2.

Sanchez CJ, Akers KS, Romano DR, Woodbury RL, Hardy SK, Murray CK, Wenke JC. (2014) D-Amino Acids Enhance the Activity of Antimicrobials Against Biofilms of Clinical Wound Isolates of Staphylococcus aureus and Pseudomonas aeruginosa. Antimicrob Agents Chemother. May 19. pii: AAC.02468-14. [Epub ahead of print]

Akers KS, Mende K, Cheatle KA, Zera WC, Yu X, Beckius ML, Aggarwal D, Li P, <u>Sanchez CJ</u>, Wenke JC, Weintrob AC, Tribble DR, Murray CK; Infectious Disease Clinical Research Program Trauma Infectious Disease Outcomes Study Group. (2014) Biofilms and persistent wound infections in United States military trauma patients: a case-control analysis. BMC Infect Dis. 2014 Apr 8;14:190. doi: 10.1186/1471-2334-14-190.

Cardile AP, <u>Sanchez CJ</u>, Samberg ME, Romano DR, Hardy SK, Wenke JC, Murray CK, Akers KS. Human plasma enhances the expression of Staphylococcal microbial surface components recognizing adhesive matrix molecules promoting biofilm formation and increases antimicrobial tolerance In Vitro. BMC Res Notes. 2014 Jul 17;7:457.

Cardille AP, <u>Sanchez CJ</u>, Hardy SK, Romano DR, Hurtgen BJ, Wenke JC, Murray CK and Akers KS. Dakin solution alters macrophage viability and function. J Surg Res. 2014 Jul 18. pii: S0022-4804(14)00656-8.

b) Books, book chapters, other publications

N/A

c) Manuscripts in preparation, manuscripts submitted

Homeyer D, <u>Sanchez CJ</u>, Mende K, Beckius ML, Akers KS, Wenke JC, Murray CK. In Vitro Toxicity and Activity of Tea Tree Oil on Filamentous Fungi and Human Cells. (*Manuscript In Revision, Journal of Medical Mycology,*)

Ward CL, Sanchez CJ, Pollet B, Romano DR, Becerra S, Hardy SK, Rathbone CR and Wenke JC. Biofilm-derived Soluble Factors of Wound Pathogens Modulate Human Bone Marrow-derived Stromal Cell Multi-lineage Differentiation, Migration, Angiogenesis, and Cytokine Secretion (Manuscript In Revision PLoS One 2014)

Harmata AJ, <u>Sanchez CJ</u>, Zienkiewicz KJ, Elefteriou F, Wenke JC and Guelcher SG. Local Delivery of D-Amino Acid Biofilm Dispersal Agents Does not Inhibit Bone Healing *In Vivo (Manuscript Submitted Clinical Orthopaedics and Related Research 2014)*

White B, Sanchez CJ, Mende K, Beckius ML, Akers KS, Wenke JC, and Murray CK. *In Vitro* Toxicity and Activity of Medical Grade Honey on Filamentous Fungi and Human Cells (Manuscript in preparation for Journal of Orthopaedic Trauma)

Sanchez CJ, Ward CL, Romano DR, Hardy SK, Becerra S, Guelcher SA, and Wenke JC. Local Delivery of D-Amino Acids from Hydrogels Disperses Biofilms In vitro and Reduces Bacterial Contamination in Wounds. (Manuscript in Preparation for submission to Journal of Wound Repair and Regeneration)

Hardy SK, Cardille AP, Akers KS, Murray CK, Wenke JC and **Sanchez CJ**. Preclinical evaluation of Rifamycins for Treatment of Staphylococcal aureus Biofilms (Manuscript in Preparation for Clinical Orthopaedics and Related Research)

Allen K, Sanchez CJ, Homeyer D, Romano DR, Hardy SK and Akers KS. Voriconazole Enhances Osteogenic Activity of Human Osteoblasts In vitro. (Manuscript in Preparation for Antimicrobial Agents and Chemotherapeutics)

Cardille AP, Woodbury RW, Hardy SK, Becerra S, Albach AM, Akers KS, Wenke JS and Sanchez CJ. Antibiofilm Activity of Norspermidine Against Clinical Orthopaedic Isolates. (Manuscript Submitted to BMC Microbiology)

Albach AM, Hardy SK, Chang DC, Garcia RG, Cardile AP, Wenke JC and Sanchez CJ. Antimicrobial Activity of Gallium and Zinc Meso- and Protoporphyrins against Biofilms of Clinical Isolates of *Staphylococcus aureus* (Manuscript In Progress)

Chang DC, Garcia RG, Hardy SK, Akers KS, Wenke JC and Sanchez CJ. Antimicrobial Activity of Gallium and Zinc Meso- and Protoporphyrins against Biofilms of Clinical Isolates of Multidrug-Resistant *Acinetobacter baumannii* (Manuscript In Progress)

10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.

Composition with biofilm dispersal agents; Publication number W02014026052 A1 2013

11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

N/A

Domestic

Carlos J. Sanchez Jr., Desiree R Romano, Kevin Akers, Ronald Woodbury, Catherine L. Ward, and Joseph C Wenke. *D-Amino Acids Enhance the Effect of Antibiotics on Bacterial Biofilms In Vitro*. American Society for Microbiology (ASM) General Meeting. San Francisco, CA. June 15-19, 2012.

Carlos J. Sanchez Jr. Biofilm-Derived Factors Reduce Viability, Inhibit Mineralization, and Differentially Regulate OPG/RANK-L in Human Osteoblasts (Invited Speaker). Military Health Research Science Symposium (formerly ATACC) Ft. Lauderdale, FL. August 13-16, 2012.

Carlos J. Sanchez Jr., Catherine L. Ward, Desiree R. Romano, Sharanda S. Hardy, Brady J. Hurtgen, Ronald Woodbury, Alex V. Trevino, Christopher R. Rathbone, and Joseph C. Wenke. *Biofilm-derived Soluble Factors Differentially Regulate RANK-L/OPG Gene Expression, Decrease Osteoblast Viability, and Inhibit Osteogenic Differentiation.* American Society for Microbiology (ASM) Conference on Biofilms. Miami, FL. September 29-October 4, 2012.

Carlos J. Sanchez Jr. Anti-Biofilm Strategies for the Treatment of Chronic Orthopaedic Extremity Infections (Invited Speaker). Extremity War Injuries VIII: Sequelae of Combat Injuries. February 11-13, 2013. Washington, DC

Carlos J. Sanchez Jr., Desiree R. Romano, Sharanda S. Hardy, Ronald Woodbury, and Joseph C. Wenke. Modulation of Angiogenesis by Biofilms of Clinical Wound Isolates. American Society for Microbiology (ASM) General Meeting. Denver, CO. May 18-21, 2013.

Carlos J Sanchez Jr, Edna M Prieto, Chad A Kruger, Katarina J Zienkiewicz, Desiree R. Romano, Scott A Guelcher, and Josh C Wenke. Development of a Biofilm Dispersive Graft for the Treatment of Contaminated Bone Defects. Gordon Research Conferences: Bones & Teeth-Translating Signaling Mechanisms into Therapy, January 26-31 2014Galveston, TX

12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars.

NA

13) PROFESSIONAL AWARDS RECEIVED DURING TENURE

NA

14) POST-TENURE POSITION / JOB TITLE

Extension of Current position, through Oak Ridge National Laboratory (ORAU)

15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION

US ARMY Institute of Surgical Research 3698 Chambers Pass Ft. Sam Houston, TX 78234 Staff Scientist

16) POST-TENURE POSITION STATUS / CATEGORY	Please indicate only one.
Permanent position at the NRC host agency	Research/Administrative position with another U.S.
Contract or temporary position at the NRC host A	gency government agency
Abbreviate Host Laboratory/Center ARMC-USAISR	Research/Administrative position with a foreign-

Research/teaching position at a U.S. college or university Self-employed/consulting Research/seaching position at a foreign college or university Other (Ptease specify, possible) Research/administration position in private industry outside of No information provided		signature required; load a scanned	Maria Crocco: Asha Davis: Linda Sligh: Peggy Wilson:	mcrocco@ adavis@na Isligh@nas pwilson@r	nas.edu is.edu .edu	via e-mail (to your NRC	, Program Coordi	nator
Research/teaching position at a U.S. college or university Research/teaching position at a foreign college or university Prostdectoral research Research/administration position in private industry in the U.S. Other (Ptease specify, possible) Research/administration position in private industry outside of No information provided the U.S. 177 APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM On a scale of 1 – 10 (poor - excellent), please rate the following: SHORT TERM VALUE Development of knowledge, skills, and research productivity Comments: In addition to expanding my research skill sets to include other bacterial agents and filamentous fungi, this opporturgiven me an appreciation and knowledge to conduct research in orthopaedics, using various animal and in vitro me antimicrobial susceptibility testing, including a variety of antimicrobial and antiseptics, as well as an introduction i biomaterials. LONG TERM VALUE How the NRC Associateship award affected your career to date Comments: This opportunity has been a great experience overall that has introduced me to areas of research, in which I can apprevious specialization into, and that I will likely further pursue upon the completion of this tenure. LAB SUPPORT Quality of support from the Laboratory-equipment, funding, orientation, safety and health guidelines, etc. Comments: Every effort was made to ensure that all necessary equipment and research reagents required for the completion of projects were readily available. Additionally, there was tremendous support from the research staff and ADVISER/MENTOR SUPPORT Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable) Comments NRC SUPPORT Quality of administrative support from the Laboratory (e.g., NIST, NRL, IWR, FHWA) NRC Program Representative Comments NRC SUPPORT Quality of administrative support please assess respective NRC aspects (e.g., moving company, insurance, Omega, percordinator, travel, etc.) Comments NRC SUPPORT Quality of administrative support staff was always very hel									
Research/teaching position at a U.S. college or university Self-employed/consulting Research/teaching position at a foreign college or university Postdoctoral research Research/administration position in private industry in the U.S. Other (Please specify, possible) Research/administration position in private industry outside of No information provided the U.S.	Quali Comi NRC SUP 10 Quali coordinate Comi Durin Every	ty of administrative supments PPORT ty of administrative supor, travel, etc.) ments g my tenure the experience in on the support s	oport. Please assessences in all aspects	s respective	NRC aspects	(e.g., moving	g company, ins	surance, Omega, pa upport, was excelle	ayroll, ent.
Research/teaching position at a U.S. college or university	Quality Common My m while	ty of mentoring from the ments nentor had an open doo not directly micro-ma	e Laboratory NRO	ys made the				rojects and provide	support
Research/teaching position at a U.S. college or university Research/teaching position at a foreign college or university Research/administration position in private industry in the U.S. Other (Please specify, possible) Research/administration position in private industry outside of the U.S. 17) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM On a scale of 1 – 10 (poor - excellent), please rate the following: SHORT TERM VALUE Development of knowledge, skills, and research productivity Comments: In addition to expanding my research skill sets to include other bacterial agents and filamentous fungi, this opportugiven me an appreciation and knowledge to conduct research in orthopaedics, using various animal and in vitro mo antimicrobial susceptibility testing, including a variety of antimicrobial and antiseptics, as well as an introduction i biomaterials. LONG TERM VALUE How the NRC Associateship award affected your career to date Comments: This opportunity has been a great experience overall that has introduced me to areas of research, in which I can appreciate the comments of the position of the production of the	10 Qualit Comu Every	ty of support from the I ments: veffort was made to en	sure that all neces	ssary equipn	nent and resea	arch reagents	required for	the completion of	research
Research/teaching position at a U.S. college or university Research/teaching position at a foreign college or university Research/administration position in private industry in the U.S. Other (Please specify, possible) Research/administration position in private industry outside of the U.S. No information provided the U.S. The proof of the following: SHORT TERM VALUE Development of knowledge, skills, and research productivity Comments: In addition to expanding my research skill sets to include other bacterial agents and filamentous fungi, this opportugiven me an appreciation and knowledge to conduct research in orthopaedics, using various animal and in vitro mo antimicrobial susceptibility testing, including a variety of antimicrobial and antiseptics, as well as an introduction in	9 How to Comp	the NRC Associateship nents: opportunity has been a	great experience	overall that	has introduce	d me to areas he completio	s of research, n of this tenu	in which I can app re.	ly my
Research/teaching position at a U.S. college or university Research/teaching position at a foreign college or university Postdoctoral research Research/administration position in private industry in the U.S. Other (Please specify, possible) Research/administration position in private industry outside of No information provided the U.S. 17) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM	Devel Comr In add given antim	opment of knowledge, nents: lition to expanding my me an appreciation and icrobial susceptibility to	research skill sets	s to include	other bacteria	aedics, using	various anim	nal and in vitro mo	dels,
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government agency Research/administration position with a non profit	Research/te Research/te Research/ac Research/ac	eaching position at a U. eaching position at a for dministration position	reign college or u in private industry	niversity in the U.S.	Self-emp Postdocte Other (Ple	loyed/consul oral research case specify, pos	ting	rith a non profit	

Rev. Nov. 2013

Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) Associate Last or Family Name		First Name M.I.			
Ston	ier		Spencer		W
2) FORWARDING Address (to which your tax statement will be mailed)		FORWARDING Phone(s) and E-Mail (if known) Home Phone: Alt. Phone: Preferred E-mail:			
3) <i>To</i>	day's Date				
27 J	une 2014			to 30 June 2014	
4)	Host Agency	Laboratory or Center		Division / Directorate / Departme	ent
	MRMC	USAMRIID		Virology	
_	(e.g., AFRL)	(e.g., Wright Patterson AFB)		(e.g., High-Speed Propulsion)	
5) <i>No</i>	ame of Laboratory NRC Advis	ser (and USMA Mentor, if applicable)			
J	ohn Dye				

6) TITLE OF RESEARCH PROPOSAL

Determination of the requirements for B cell and CD8 T cell responses in protection against Ebolavirus infection after VRP-GP vaccination

- 7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.
 - 1) Antibody responses appear to be most acutely responsible for protection against filovirus infection after vaccination
 - 2) CD8 T cells may contribute to protection but it varies by mouse strain slightly
 - 3) Both CD4 and CD8 T cell responses to Ebola glycoprotein are detectable after VRP vaccination
 - 4)
 - 5)

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

My current projects involve further describing VRP immune responses and components of the immune system that are involved. Additionally I am involved in a team that is evaluating memory immune responses in filovirus outbreak survivors in Uganda. Recently the lab was awarded an NIH grant to evaluate antibody therapeutics and I am involved in this effort as well.

- 9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH
 - Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.
 - a) Publications in peer-reviewed journals

Herbert AS, Kuehne AI, Barth JF, Ortiz RA, Nichols DK, Zak SE, <u>Stonier SW</u>, Muhammad MA, Bakken RR, Prugar LI, Olinger GG, Groebner JL, Lee JS, Pratt WD, Custer M, Kamrud KI, Smith JF, Hart MK, and Dye JM. "Venezuelan equine encephalitis virus replicon particle vaccine protects nonhuman primates from intramuscular and aerosol challenge with ebolavirus." 2013. *J Virol*. 87: 4952-64.

- b) Books, book chapters, other publications
- c) Manuscripts in preparation, manuscripts submitted
- 10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.

Í	PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location. International
<u>S</u> N	Domestic Spencer W. Stonier, Andrew S. Herbert, Ariel Sobarzo, Ana I. Kuehne, Yael Eskira, Julius Lutwama, Leslie Lobel, and John M. Dye. T and B cell memory responses in 2012 filovirus outbreak survivors. American Association of Immunologists Annual Meeting. Pittsburgh, PA 2014.
	SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES Include dates, names and locations of seminars
	Antibody and memory T cell responses in <i>Ebolavirus</i> and <i>Marburgvirus</i> outbreak survivors. MD Anderson Cancer Center, April 2014
13) I	PROFESSIONAL AWARDS RECEIVED DURING TENURE
	POST-TENURE POSITION / JOB TITLE Research Scientist
ĺ	IAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION USAMRIID 1425 Porter St Ft Detrick, MD 21702
	Post-Tenure Position at the NRC host agency Contract or temporary position at the NRC host Agency Abbreviate Host Laboratory/Center USAMRIID Research/Administrative position with another U.S Research/Administrative position with a foreign- Research/Administrative position at a U.S. college or university Research/teaching position at a foreign college or university Research/administration position in private industry outside of the U.S. Research/administration position in private industry outside of the U.S. Research/administration position with a non profit postdoctoral research Research/administration position with a non profit postdoctoral research Research/teaching position at a U.S. college or university Research/teaching position at a foreign college or university
expe	For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DUIRNG TENURE Itemize riences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also ize what you have done to share your culture with your colleagues and the community.
1 2 3 4 5	
On	APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM a scale of 1 – 10 (poor - excellent), please rate the following: SHORT TERM VALUE Development of knowledge, skills, and research productivity Comments LONG TERM VALUE
	How the NRC Associateship award affected your career to date Comments LAB SUPPORT Quality of support from the Laboratoryequipment, funding, orientation, safety and health guidelines, etc. Comments

ADVISER/MENTOR SUPPORT

Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)
Comments

LPR SUPPORT

Quality of administrative support from the <u>Laboratory</u> (e.g., NIST, NRL, IWR, FHWA) NRC <u>Program</u> <u>Representative</u> (LPR) Comments

NRC SUPPORT

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required; but you may upload a scanned signature file below:

Asha Davis: adavis@nas.edu
Linda Sligh: lsligh@nas.edu
Melanie Suydam: msuydam@nas.edu
Peggy Wilson: pwilson@nas.edu

Id# Rev. April. 2014 Proj/Act ID#

Advisers to the Nation on Science, Engineering, and Medicine National Research Council

Research Associateship Programs

FINAL REPORT

1) Associate Last or Family Name			First Name M.1			
Ward			Catherine		L	
2) <i>FO</i>	RWARDING Address (to v	which your tax statement will be mailed)	FORWARDIN	IG Phone(s) and E-Mail (if		
			known) Home	Phone:		
			Alt. Phone:			
			Preferred E-m	ail:		
3) Today's Date			Dates of Tenure			
9/2/20	014		from 8/23/201	1 to 9/5/2014		
4)	Host Agency	Laboratory or Center		Division / Directorate / Departme	nt	
	MRMC	USAISR		ETRM		
	(e.g., AFRL)	(e.g., Wright Patterson AFB))	(e.g., High-Speed Propulsion)		
5) <i>Nar</i>	me of Laboratory NRC Adv	riser (and USMA Mentor, if applicable)				
Jo	oseph C. Wenke					

6) TITLE OF RESEARCH PROPOSAL

Improving Cellular Therapies for Osseous Trauma Using Injectable Scaffolds for Bone Regeneration

7) SUMMARY OF RESEARCH DURING TENURE Itemize significant findings in concise form, utilizing key concepts/words.

- 1) Utilized and optimized an injectable polyurethane (PUR) matrix for delivery of cells (bone marrow mesenchymal stem cells, BMSCs) and osteogenic agents (Lovastatin, LV) for a bone regeneration therapy in collaboration with Dr. Scott Guelcher (Vanderbilt University).
- 2) Developed methods to encapsulate cells in alginate matrices for survivability during PUR curing.
- 3) Analyzed cell fate within injectable scaffolds (PUR). *In vitro* analysis included determining viability, attachment and proliferation of cells onto the scaffolds in culture. *In vivo* analysis included determining cell survivability after injection in a rat calvarial defect.
- 4) Investigated osteogenic potential of injectable cell delivery scaffolds with the addition of osteogenic agents in the system.

(USMA Davies Fellow: please add summary of teaching, including classes taught.)

8) RESEARCH IN PROGRESS Describe in no more than 100 words.

An optimized cell (BMSC) and osteogenic agent (Lovastatin) delivery system using an injectable polymer (polyurethane) will be tested in a rat femur segmental defect model to determine the ability to form new bone in a critical-size defect. BMSCs and Lovastatin within the injectable system have been optimized and tested *in vitro* to determine ideal concentrations to support osteogenic differentiation. This model will assess the ability of the system in a relevant model of bone regeneration.

9) PUBLICATIONS AND PAPERS RESULTING FROM NRC ASSOCIATESHIP RESEARCH

Provide complete citations: author(s), title, full name of journal, volume number, page number(s), and year of publication.

a) Publications in peer-reviewed journals

- 1) Garg K, Ward CL, Hurtgen BJ, Wilken JM, Stinner DJ, Wenke JC, Owens JG, Corona BT. Volumetric muscle loss: persistent functional deficits beyond frank loss of tissue. Journal of Orthopaedic Research, 2014
- McDaniel JS, Pilia M, Ward CL, Pollot B, Rathbone CR. Characterization and multilineage potential of cells derived from isolated microvascular fragments. Journal of Surgical Research, 2014
- 3) Corona BT, Garg K, Ward CL, McDaniel J, Walters TJ, Rathbone CR. Autologous minced muscle grafts: A tissue engineering therapy for the volumetric loss of skeletal muscle. American Journal of Physiology Cell Physiology, 2013.
- 4) Sanchez CJ, Prieto EM, Krueger CA, Zienkiewicz KJ, Romano DR, Ward CL, Akers KS, Guelcher SA, Wenke JC. Effects of local delivery of D-Amino acids from biofilm-dispersive scaffolds on infection in contaminated rat segmental defects. Biomaterials, 2013.
- 5) Sanchez CJ*, Ward CL*, Romano DR, Hurtgen BJ, Hardy SK, Woodbury RL, Rathbone CR, Wenke JC. Staphylococcus aureus biofilms decrease osteoblast viability, differentially regulate RANK-L/OPG gene expression, and inhibit osteogenic differentiation. BioMed Central Musculoskeletal Disorders, 2013.
- 6) Corona BT, Wu X, **Ward CL**, McDaniel JS, Rathbone CR, Walters TJ. The promotion of a functional fibrosis in skeletal muscle with volumetric muscle loss injury following the transplantation of muscle-ECM. Biomaterials, 2013.

b) Books, book chapters, other publications

c) Manuscripts in preparation, manuscripts submitted

- 1) Ward CL*, Sanchez CJ*, Pollot BE Romano DR, Hardy SK, Becerra SC, Rathbone CR, Wenke JC. Biofilm-derived Soluble Factors of Wound Pathogens Modulate Human Bone Marrow-derived Stromal Cell Multi-lineage Differentiation, Migration, Angiogenesis, and Cytokine Secretion. *In Preparation*.
- 2) Guo R, Ward CL, Davidson JM, Duvall CL, Wenke JC, Guelcher SA. A Transient Cell-Shielding Method for Viable MSC Delivery within Hydrophobic Scaffolds Polymerized In Situ. Biomaterials, *In preparation*.
- 3) Garg K, Ward CL, Rathbone CR, Corona BT. Transplantation of devitalized muscle scaffolds is insufficient for appreciable de novo muscle fiber regeneration after volumetric muscle loss. Cell and Tissue Research, Submitted.

10) PATENT OR COPYRIGHT APPLICATIONS RESULTING FROM NRC ASSOCIATESHIP RESEARCH Provide titles, inventors, and dates of applications.

1) Guelcher SA, Guo R, Wenke JC, Ward CL. Modified Cell Delivery System. Provisional Patent Filed. 2014

11) PRESENTATIONS AT SCIENTIFIC MEETINGS OR CONFERENCES

Provide complete references: author(s), title, abstract/proceeding citation, meeting name and location.

International

Domestic

- Ward CL, Guo R, Guelcher SG, Wenke JC. Development of a Cell Delivery Scaffold for Tissue Regeneration. Military Health Systems Research Symposium, 2014, Ft. Lauderdale FL.
- Ward CL, Ji L, Corona BT. Expanded Autologous Minced Muscle Grafts Promote De Novo Regeneration after Volumetric Muscle Loss. Military Health Systems Research Symposium, 2014, Ft. Lauderdale FL.
- 3) Ward CL, Wenke JC, Corona BT. Soft Tissue Therapies for Impaired Musculoskeletal Healing in a Rat Composite Injury Model. Orthopaedic Research Society, New Orleans, LA.
- 4) Ward CL, Guo R, Wenke JC, Guelcher, SA. Development of an Injectable and Settable Polyurethane Cell Delivery System for Tissue Regeneration. Tissue Engineering and Regenerative Medicine International Society Annual Meeting Americas, 2013, Atlanta, GA.
- 5) Ward CL, Wenke JC, Corona BT. Impaired Musculoskeletal Healing in a Rat Composite Injury Model. Tissue Engineering and Regenerative Medicine International Society Annual Meeting Americas, 2013, Atlanta, GA.
- 6) Scott J, Corona BT, Ward CL, Harrison BS, Saul J, Christ GJ. Development of a Novel Tissue Engineered Muscle Repair Contruct with potential for Enhanced Motor End Plate Formation and Function. Tissue Engineering and Regenerative Medicine International Society Annual Meeting – Americas, 2013, Atlanta, GA.
- 7) Ward CL, Sanchez CJ, Woodbury R, Rathbone C, Wenke JC. Soluble biofilm-derived factors of *S. aureus* and *P. aeruginosa* reduce the viability and multi-differential potential of human mesenchymal stem cells. Military Health Systems Research Symposium, 2012, Ft. Lauderdale FL.

12) SEMINARS OR LECTURES DELIVERED AT UNIVERSITIES AND/OR INSTITUTES—Include dates, names and locations of semina

13) PROFESSIONAL AWARDS RECEIVED DURING TENURE

14) POST-TENURE POSITION / JOB TITLE

Staff Scientist

15) NAME AND ADDRESS OF POST-TENURE POSITION / JOB ORGANIZATION

United States Army Institute of Surgical Research 3698 Chambers Pass Fort Sam Houston TX 78234

16) POST-TENURE POSITION STATUS / CATEGORY Please indicate	e only one.
Permanent position at the NRC host agency	Research/administration position in private industry in the U.S.
Contract or temporary position at the NRC host Agency	Research/administration position in private industry outside of
Abbreviate Host Laboratory/Center <u>USAISR</u>	the U.S.
Research/Administrative position with another U.S	Research/administration position with a non profit
government agency	Self-employed/consulting
Research/Administrative position with a foreign-	Postdoctoral research
government agency	Other (Please specify, possible)
Research/teaching position at a U.S. college or university	No information provided
Research/teaching position at a foreign college or university	

17) (For J-1 visa holders only) SUMMARY OF CULTURAL AND EDUCATIONAL EXCHANGE DUIRNG TENURE Itemize experiences that your laboratory (LPR and/or Adviser) has offered to you that facilitated your learning about American culture. Also itemize what you have done to share your culture with your colleagues and the community.

- 1)
- 2)
- 3)
- 4)
- 5)

18) APPRAISAL OF RESEARCH ASSOCIATESHIP PROGRAM

On a scale of 1 - 10 (poor - excellent), please rate the following:

SHORT TERM VALUE

Comments

Development of knowledge, skills, and research productivity

As an NRC fellow, I was able to lead a project with the opportunity to contribute to grants on the project. I was also able to be involved in several other projects in the lab, which led to collaborations and publications.

LONG TERM VALUE

Comments

How the NRC Associateship award affected your career to date

The associateship has progressed my career through experience in the field and also through very valuable networking internally and externally.

LAB SUPPORT

Quality of support from the Laboratory-equipment, funding, orientation, safety and health guidelines, etc.

Comments

Despite a learning curve with government laboratories (ordering, finances, etc.), the facilities were amazing and extremely helpful in accelerating the project.

ADVISER/MENTOR SUPPORT

Quality of mentoring from the Laboratory NRC Adviser (USMA Mentor, if applicable)

Comments

The NRC Advisor was always constructive and helpful. He aided in mentoring me through my project while also facilitating several opportunities for collaborations with other projects.

LPR SUPPORT

Quality of administrative support from the <u>L</u>aboratory (e.g., NIST, NRL, IWR, FHWA) NRC <u>Program Representative</u> (LPR)

The LPR was very helpful and supportive of my actions as an NRC fellow.

Quality of administrative support. Please assess respective NRC aspects (e.g., moving company, insurance, Omega, payroll, Program Coordinator, travel, etc.)

Comments

The NRC admin was very attentive to any issues I had.

18) PLEASE PROVIDE ANY SUGGESTIONS FOR PROGRAM IMPROVEMENT.

Please do NOT scan to PDF. Send the Final Report as MSWord document via e-mail to your NRC Program Coordinator

No handwritten signature required;

alu aul

but you may upload a scanned

signature file below:

Asha Davis: adavis@nas.edu lsligh@nas.edu Linda Sligh: Melanie Suvdam: msuvdam@nas.edu Peggy Wilson: pwilson@nas.edu

Rev. April. 2014 Id# Proj/Act ID#